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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,974	OTSU ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-20* is/are pending in the application.

4a) Of the above claim(s) *5-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0506*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 7, 13, and 15-20 are pending.

Applicants' response of July 25, 2007 is acknowledged.

The following Election/Restriction Requirement replaces the Election/Restriction Requirement mailed June 25, 2007.

Election/Restrictions

Restriction is required under 35 U.S.C. 121.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, Claims 7, 13, and 15, drawn to a method of screening for an agent useful for treatment of cardiac failure.

Group II, Claims 16-19, drawn to a method for treatment of cardiac failure.

Group III, Claim 20, drawn to a method for diagnosing cardiac failure.

For each of Inventions I-III above, restriction to one or more of the following is also required under 35 USC 121. Therefore, election is required of one of Inventions I I-III and one or more of Inventions (A)-(I), as follows.

If Invention I is elected, elect one of:

(A) Inhibition of ASK1 activity/autophosphorylation assay
(B) Inhibition of ASK1 transcription/translation assay
(C) Inhibition of a ASK1 activating factor
(D) Inhibition of a factor activated by ASK1

If (C) is elected, elect one of:

(i.) Daxx
(ii.) TAF2
(iii.) Calmodulin-dependent kinase II

If (D) is elected, elect one of:

(iv.) MKK3
(v.) MKK4

(vi.) MKK6
(vii.) MKK7
(viii.) JNK
(ix.) p38 MAPK

If Invention II is elected, elect one of:

(E) Inhibiting expression of ASK1
(F) Inhibiting ASK1-induced apoptosis
(G) Inhibiting ASK1 activity/autophosphorylation
(H) Inhibiting ASK1 transcription
(I) Inhibiting ASK1 translation

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: The technical feature linking Groups I-III appears to be that the all related to ASK1. However, ASK1 was known in the art. For example, Gilot et al, 2002 teach a method for identifying inhibitors of ASK1, which anticipates Claim 7. Therefore Groups I-III share no special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Furthermore, the methods of Groups III do not use the same reagents or produce the same results. Accordingly, Groups I-III are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

Searching more than one of Groups I-III would represent a burden on the Office for the following reasons. A search for any one of the methods of Groups I-III would not encompass a search for any other said methods because the methods do not share a special technical feature of steps and products used, or results produced. Thus, the search for more than one of Groups I-III would be a burden on the Office.

These inventions lack Unity of Invention for the reasons given above. Furthermore, each invention has acquired a separate status in the art due to their recognized divergent subject matter and, thus, searching more than one invention would be a burden on the Office. Therefore, restriction for examination purposes, as indicated, is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

First Action on the Merits

During a telephone conversation with Brian Wong on September 20, 2007 a provisional election was made, with traverse, to prosecute the invention of Group I, sub-invention (B). The elected invention is directed to a method for identifying an agent useful for treating cardiac failure, wherein the method analyzes ASK1 activity or autophosphorylation. Affirmation of this election must be made by Applicants when replying to this Office action.

In support of their traversal Applicants argue, in their response of July 25, 2007, that all of the claims require the feature of inhibiting the function of ASK1, which is not disclosed by the prior art. This argument is not found to be persuasive. Invention III does not require of inhibiting the function of ASK1, thus said feature is not feature that links all claims. Moreover, methods inhibiting the function of ASK1 were known in the art (Ichijo et al, 1997, Fig 4; IDS). Therefore, the feature of inhibiting the function of ASK1 is not a special technical feature. The restriction requirement is deemed to be proper.

Claims 7, 13, and 5-20 are pending. Claims 13 and 5-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claim 7 is hereby examined.

Priority

The priority date granted for the instant invention is July 28, 2004, the filing date of PCT/JP04/11124, which disclosed the elected invention. If Applicants which to perfect their claim to priority to JP 2003-281281, filed July 28, 2003, an English-language translation of said application should be filed.

Information Disclosure Statement

The Information Disclosure Statement filed May 1, 2004 lists JP10-000093. Said foreign patent document has not been considered. If Applicants wish for said foreign patent document to be considered, and English-language translation thereof should be submitted. Any subsequent rejection, based on consideration of said English-language translation, will not be considered a new grounds for rejection.

Title

The title is objected to because it is not descriptive of the elected invention.

Abstract

The abstract is objected to because it is too long.

MPEP 608.01(b) states

> The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Claims-Objections

The claim set is objected to for not beginning with a sentence of which the claims are an object e.g., "We claim" or "The claims are".

Claim 7 is objected to for reciting non-elected subject matter.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Claim 7 is directed to a method. However, no steps are set forth by which to practice said method. The skilled artisan would not be apprised of the metes and bounds of the recited invention.

For Claim 7, the term "ASK1" renders the claim indefinite. The structural limitations provided by the specification for said term are only exemplary (parg bridging pg 6-7); moreover no functional limitations are provided by the specification for said term. Therefore, the skilled artisan would not be apprised of the metes and bounds of the recited invention.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying agents that affect the kinase activity of ASK1 using cells expressing the ASK1 taught by Saitoh et al, 1998 (IDS), does not reasonably provide enablement

for identifying agents that affect the kinase activity of any ASK1 having any structure, wherein the ASK1 affects cardiac function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claim 7 is so broad as to encompass any method for identifying agents that affect the kinase activity of any ASK1, wherein the ASK1 has any structure, and wherein the ASK1 affects cardiac function. The scope of this claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired apoptotic activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are

conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to identifying agents that affect the kinase activity of the ASK1 taught by Saitoh et al, 1998.

While methods for analyzing kinase activity and cardiac function are known, it is not routine in the art to screen an essentially unlimited number of proteins for kinase activity and effect on cardiac function. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification also does not support the broad scope of Claim 7, which encompasses any method for identifying agents that affect the kinase activity of ASK1 and ASK1-mediated cardiac function, wherein the ASK1 has any structure. The specification does not support the broad scope of Claim 7 because the specification does not establish: (A) the structure of ASK1 proteins that have kinase activity and regulate cardiac function; (B) regions of the protein structure which may be modified without affecting the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of methods for identifying agents that affect the kinase activity of ASK1, wherein the ASK1 has any structure, and wherein the ASK1 affects cardiac function. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claim 7 is are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

This claim is directed to a genus of methods for identifying agents that affect the kinase activity of any ASK1 having any structure, wherein the ASK1 affects cardiac function. The specification teaches only a single representative species of such methods. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a means to identify agents that affect the kinase activity of any ASK1 having any structure, wherein the ASK1 affects cardiac function. Given this lack of description of representative species encompassed by the genus of the claim, the

specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hirotani et al, 2002 in view of Saitoh et al, 1998 as evidence by Sorescu et al, 2002. Hirotani et al teach that ASK1 mediates reactive oxygen species (ROS)-stimulated cardiac hypertropy. As evidence by Sorescu et al, said ROS-stimulated cardiac hypertrophy leads to left ventricular hypertrophy and heart failure (Abstract). Neither Hirotani et al nor Sorescu et al teach a method for assaying ASK1 activity. Saitoh et al teach methods for assaying ASK1 kinase activity and identifying inhibitors of said activity (Fig 2; pg 2602, parg 4). It would have been obvious to a person of ordinary skill in the art to use the methods of Saitoh et al to identifying inhibitors of ASK1 activity in cardiac cells. Motivation to do so derives for the desire to screen for drugs useful in the prevention or treatment of cardiac failure. The expectation of success is high, as methods for assaying identifying inhibitors of the ASK1 taught by Saitoh et al were known in the art. Therefore, Claims 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hirotani et al, 2002 in view of Saitoh et al, 1998 as evidence by Sorescu et al, 2002.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER

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